

What is claimed is:

1. A method of obtaining a primary-result peptide having at least one binding domain that

binds a predetermined dynamic target material at a non-active site

5 wherein said dynamic target material has at least two conformational energy-minima states comprising:

(a) accessibly-conformationally restraining said dynamic target material in substantially a single conformational energy-minima state

(b) affinity-exposing said accessibly-conformationally restrained single conformational energy-minima dynamic target material to a peptide library comprising inquiry-peptides and identifying peptide which associate with the target with sufficient affinity to withstand washing at least about 4 times in rapid succession with a standard buffer containing physiologically balanced salt solution and a non-ionic detergent (<0.1% v/v) ("peptide hits").

(c) affinity-exposing said accessible conformationally-restrained single conformational energy-minima state dynamic target material to said peptide library wherein said single conformational energy-minima state is substantially a single energy-minima state other than the state of step (a) and identifying peptide-hits; and

(d) selecting at least one peptide-hit that inhibits target function by other-than-competitive inhibition the target material, which peptide-hit being a primary-result peptide.

2. A method of obtaining a primary-result peptide having at least one binding domain wherein said binding domain is a low affinity binding domain comprising:

(a) preparing a target polypeptide, as a fusion protein having a known target region and an inquiry target region wherein the known target region is linked to the inquiry target region by a flexible linker;

(b) preparing a tandem peptide display library where said tandem peptides comprise

(i) a known peptide element having a binding domain of low affinity as to said known target region said element connected to

(ii) a flexible linker said flexible linker connected to

(iii) an inquiry peptide sequence

(c) affinity exposing said target protein to said peptide library;

(d) identifying tandem peptide-hits ;

5 (e) identifying said inquiry peptide sequence of said tandem peptide hit as a primary result peptide.

3. The method of Claim 2 wherein the known target region of (a) comprises an SH3 domain and the known peptide of step (b)(i) comprises a prolein-rich SH3 binding domain

10 having an affinity for the known target region with an affinity in the range of 100 micromolar, so as to be of sufficiently low affinity to substantially dissociate from the known target region after washing at most about 4 times in rapid succession with a standard buffer containing physiologically balanced salt solution and a non-ionic detergent (<0.1% v/v).

15 4. The method of Claim 2 wherein the flexible linker of step (b)(ii) is a short peptide.

5. A method of obtaining a primary-result peptide useful in inducing formation of activated-like multiprotein complexes bridging two partner polypeptides comprising:

20 (a) anchoring to a substratum a target polypeptide having a known dimerizable target region, said anchoring being at a location other than said target region and assembling the multiprotein complex, as a ternary complex, by adding a partner target polypeptide and cognate-like accessory polypeptide which bridges the two partner polypeptide targets;

(b) exposing said substratum anchored activated-like multiprotein complex to a phage peptide display library and

(c) selecting phage that bind the assembled protein-protein complex with sufficient affinity to withstand washing four times in rapid succession with a standard buffer

5 containing physiologically balanced salt solution and a non-ionic detergent (<0.1% v/v)

(d) selecting from among said complex binding phage a phage that when added to a system containing a substratum anchored target polypeptide and a partner target polypeptide, is capable of inducing the formation of the multiprotein complex such that the two target polypeptide partners become associated in the absence of the accessory polypeptide, said phage
10 bearing a primary result peptide.

6. A method of preparing an enhanced peptide display library comprising
preparing a tandem peptide display library having a known target region and an inquiry
target region where said tandem peptides comprise

15 (i) a known peptide element having a binding domain of low affinity as to said
known target region said element connected to

(ii) a flexible linker said flexible linker connected to

(iii) an inquiry peptide sequence

(iii) wherein said inquiry peptide sequence is further connected to a bacteriophage
20 structural protein.

7. A library of the method of Claim 6.

8. An enhanced peptide display library comprising a tandem peptide display library having a known target region and an inquiry target region where said tandem peptides comprise

(i) a known peptide element having a binding domain of low affinity as to said known target region said element connected to

5 (ii) a flexible linker said flexible linker connected to

(iii) an inquiry peptide sequence

(iii) wherein said inquiry peptide sequence is further connected to a bacteriophage structural protein.